PIGMENTATION

KERATINOCYTE-DERIVED IL-15 EXACERBATES MELANOCYTES IMMUNOLOGIC DESTRUCTION IN VITILIGO

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Introduction: Both excessive oxidative stress and abnormal CTL-dependent auto-immunological activation contribute to melanocyte degeneration in vitiligo. Whether oxidative stress regulates expression of IL-15 and pathological role of IL-15 in the vitiligo has not been sufficiently elucidated.

Objective: To investigate function and mechanism of IL-15 in the melanocytes immunologic destruction in vitiligo.

Materials and Methods: qRT-PCR and immunofluorescence were performed to assessed the expression of IL-15 in vitiligo lesions. ELISA was conducted to detect the IL-15 protein level in culture supernatants and serum from patients with vitiligo. In vitro, Western blot, qRT-PCR, ELISA and flow cytometry were used to analyze the expression and regulation of IL-15 and IL-15Rα in keratinocytes exposed to H2O2. ChIP assay was used to identify the transcription of IL-15 in stressed keratinocytes. the two co-culture models of KC-CD8+T and CD8+T-melanocye were constructed to analyze the effect of IL-15 on CTL by flow cytometry.

Results: IL-15 expression obviously increased in lesions and serum from vitiligo patients. In vitro, oxidative stress apparently induced IL-15 and IL-15Rα expression by potentiating NF-κB P65 signaling. IL-15Rα mediated IL-15 membrane translocation in keratinocytes under oxidative stress. CHIP assay identified that NF-κB P65 binds to the promoter of il-15. Keratinocyte-derived IL-15 activated CTL to damage melanocytes mainly in trans-presented form, rather than soluble form, resulting in the production of IFN-γ and Granzyme B in a STAT3 and STAT5 dependent way.

Conclusions: IL-15 plays a critical role in CTL-mediated immunologic destruction of melanocytes in patients with vitiligo. Targeting the IL-15-JAK-STAT axis may be a potential novel therapeutic strategy for vitiligo treatment.